

REMARKS/ARGUMENTS

I. Status of the claims

Claims 1-20 are currently pending.

II. Interview

Applicants thank Examiners Tung and Horlick for the helpful interview on April 21, 2004. Applicants appreciate the Examiners' willingness to re-consider the patentability of the claims in view of the interview and the remarks below.

III. Rejections under 35 U.S.C. § 103

A. Rejection in view of Will et al. and Gold et al.

The Examiner rejected the claims as allegedly obvious in view of Gold *et al.* and Will *et al.* In the previous Office Action, the PTO acknowledged that Will does not teach or suggest the use of 2'-O-methyl nucleotides, 2'-fluoro-nucleotides, and 2'-amino nucleotides in its nucleic acid reaction. However, the PTO asserted that because Gold teaches 2'-O-methyl nucleotides, 2'-fluoro-nucleotides, and 2'-amino nucleotides, it would have been *prima facie* obvious to apply Gold *et al.*'s modified nucleotides to Will's kits and methods for carrying out a nucleic acid amplification reaction.

In response, Applicants argued that there was no motivation in the art to combine the references and further that there was no reasonable expectation of success. In the final Office Action mailed January 2, 2004, the Examiner argued that the claims did not require modification of nucleotides on their sugar. Moreover, the Examiner argued that Gold *et al.* disclosed that polynucleotides with modified nucleotides has increased affinity for a "target," thereby allegedly providing a motivation to combine the two references. Applicants respectfully traverse the rejection.

First, Applicants note that the Examiner acknowledged in the interview that the comments regarding the scope of the claims were incorrect. Specifically, the claim language is

directed to nucleotides modified on the 2' oxygen of their sugar or that comprise arabinose as the sugar.

Second, the Gold reference is directed to identifying affinity for *proteins*. In particular, Gold teaches the use of modified nucleotides to synthesize RNA molecules that have reduced affinity for HIV-RT and are resistant to enzymatic and chemical degradation (Gold, page 10, paragraph number 104, page 13, paragraph number 138, page 16, paragraph number 163 and page 17, paragraph number 168). Applicants note that nowhere does Gold even mention a nucleic acid amplification reaction. Applicants submit that the PTO has provided no evidence that one of skill in the art would select nucleotides modified at the sugar for use in Will's methods. Applicants submit instead that when looking for substitution for modified nucleotides in Will's methods, one of ordinary skill in the art would select those nucleotides with ability to interfere with base pairing according to Will, *i.e.*, those with modified bases. Applicants therefore respectfully submit that the PTO has not provided sufficient motivation for one of ordinary skill in the art at the time the invention was made to apply Gold's modified nucleotides to Will's kits and methods.

Moreover, the PTO has provided no evidence that one of ordinary skill in the art would have had a reasonable expectation of success using the combination suggested by the PTO. The PTO has not provided any evidence that Gold's modified nucleotides (modified on the sugar backbone instead of on the base) would have been expected to possess the same properties or function in the same way as the modified nucleotides in Will's kits. Specifically, the PTO has failed to provide any evidence that applying Gold's modified nucleotides to Will's methods would reduce, rather than increase, non-specific amplification. In fact, the PTO has not provided any evidence in Will or Gold or in the art that those of ordinary skill would have expected Gold's modified nucleotides to have any effect on non-specific amplification at all.

As there is no motivation or suggestion to combine the teachings of Will and Gold, and as there is no reasonable expectation that the combination would succeed, the PTO has failed to establish a *prima facie* case of obviousness against independent claims 1 and 11. Claims 2-4, 6-8, and 10 depend from claim 1 and claims 12-14, 16-18 and 20 depend from claim

11. The references are therefore not sufficient to establish a *prima facie* case of obviousness against Claims 1-4, 6-8, 10-14, 16-18 and 20.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection of Claims 1-4, 6-8, 10-14, 16-18 and 20 under 35 U.S.C. § 103(a) as being obvious over Will in view of Gold.

B. Rejection in view of Will et al. and Gold et al. in further view of Reese

Claims 5, 9, 15 and 19 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Will in view of Gold and in further view of Reese. Applicants traverse the rejection. Applicants respectfully submit that the Patent Office has failed to meet the burden of demonstrating the required motivation and reasonable expectation of success to combine the teachings of Will, Gold and Reese, thereby failing to establish *prima facie* obviousness against Claims 5, 9, 15 and 19.

The PTO relies on the combination of Will and Gold to establish *prima facie* obviousness against independent claims 1 or 11 from which Claims 5, 9, 15 and 19 ultimately depend. The PTO acknowledged that neither Will nor Gold teaches the use of arabinose nucleotides. *See*, Office Action of March 27, 2003, page 5. However, the PTO states that Reese teaches arabinose nucleotides and alleges that one of skill in the art would have been motivated to apply Reese's modified arabinose nucleotides to Will's and Gold *et al.*'s combined kits and methods.

The PTO has not provided any motivation to apply Reese's arabinose nucleotides to Will's modified nucleic acid amplification reaction. Like 2'-O-methyl nucleotides, 2'-fluoro-nucleotides and 2'-amino nucleotides, arabinose-containing nucleotides are modified on their sugar when compared to nucleotides of naturally occurring nucleic acids. In particular, the orientation of the -H and -OH side groups of the C-2 of arabinose is altered when compared to ribose or deoxy-ribose sugars. As discussed above, the PTO has failed to provide any motivation for using a nucleotide modified on its sugar instead of on its base in Will's methods. Applicants submit that Reese does not provide the necessary motivation. Reese teaches a process for the

preparation of arabinose nucleotides. Reese does not teach or suggest anything about using arabinose nucleotides or any nucleotides with modified sugars in a nucleic acid amplification reaction, much less in Will's methods. Neither does Reese teach or suggest that arabinose nucleotides in particular or nucleotides with modified sugars in general might interfere with base pairing or reduce non-specific amplification. Accordingly, Reese cannot provide the missing motivation to apply Reese's arabinose nucleotides to Will's modified nucleic acid amplification reaction. Applicants therefore submit that the PTO cannot combine the teachings of Reese and the teachings of Will and Gold to establish a *prima facie* case of obviousness against dependent Claims 5, 9, 15 and 19.

Moreover, the PTO has failed to show that those of ordinary skill in the art would have had a reasonable expectation of success applying Reese's arabinose nucleotides to Will's methods. The PTO has not provided any evidence that those of ordinary skill in the art would have expected that Reese's arabinose nucleotides used in Will's modified nucleic acid amplification reaction would have had any effect on reducing non-specific amplification. Further, the PTO has failed to provide any evidence that those of skill in the art would have expected Reese's arabinose nucleotides to function within the three 3' terminal nucleotide positions in a modified primer as recited by the present claims.

Applicants therefore submit that even in view of Reese, the PTO has failed to provide the requisite motivation and reasonable expectation of success to apply Reese's arabinose nucleotides to Will's modified nucleic acid amplification reaction. Accordingly, Applicants submit that the PTO has not established a *prima facie* case of obviousness against dependent Claims 5, 9, 15 and 19.

In view of the foregoing, Applicants respectfully request withdrawal of the rejection of Claims 5, 9, 15 and 19 under 35 U.S.C. § 103(a) as being obvious over Will in view of Gold in further view of Reese.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

Appl. No. 10/083,233

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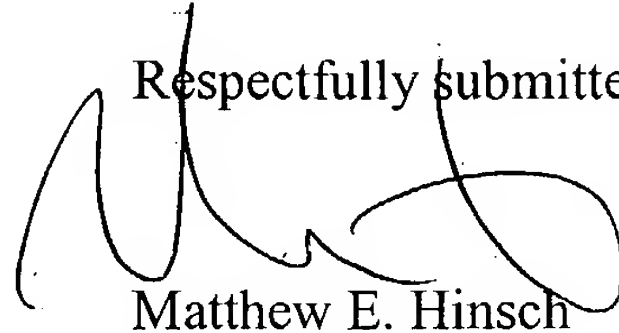
Amdt. dated May 2, 2004

Amendment under 37 CFR 1.116 Expedited Procedure

Examining Group

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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Attachments

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